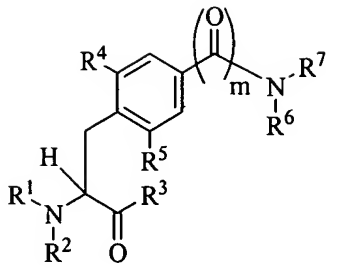
What is claimed is:

1. A compound of formula I:



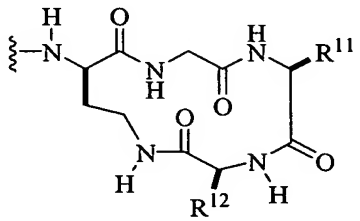
I ;

or a stereoisomer, prodrug, pharmaceutically acceptable salt, hydrate, solvate, acid salt hydrate, N-oxide or isomorphic crystalline form thereof.

wherein:

R^1 and R^2 are each, independently, H, alkyl, alkenyl, or $-C(=NH)NH_2$, provided that at least one of R^1 and R^2 is other than $-C(=NH)NH_2$, or R^1 and R^2 taken together with the nitrogen atom to which they are attached form a 4- to 8-membered heterocycloalkyl ring wherein the heterocycloalkyl ring is optionally interrupted with one additional O, N, or S heteroatom;

R^3 is $-[J]_o$-X,



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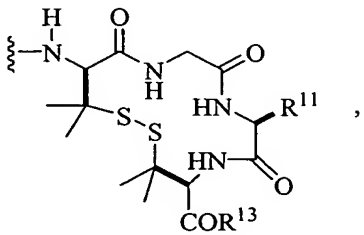

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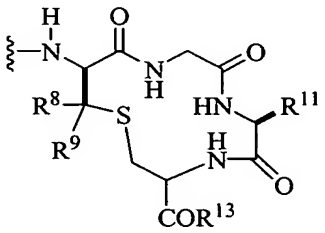

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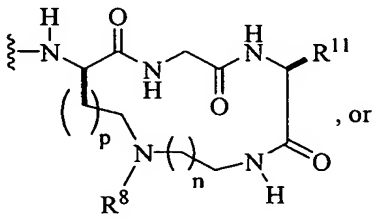

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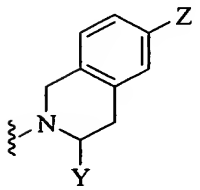


;

J is $[NR^{8a}(C(R^{9a})(R^{10}))_n\text{-}C(=O)]$;

X is OR^8, $NR^{8b}R^{9b}$, or $-N(R^{8c})CH(R^{9c})(R^{10})$;

R^4 and R^5 are each, independently, H or methyl;

R^6 and R^7 are each, independently, H or alkyl, or R^6 and R^7 taken together with the nitrogen atom to which they are attached form a 4- to 8-membered heterocycloalkyl ring wherein the heterocycloalkyl ring is optionally interrupted with one additional O, N, or S heteroatom;

R^8 and R^9 are each, independently, H or alkyl;

R^{8a} and R^{9a} are each, independently, H or alkyl, or R^{8a} and R^{9a} taken together with the nitrogen and carbon atoms through which they are connected form a 4- to 14-membered heterocycloalkyl ring wherein the heterocycloalkyl ring is optionally interrupted with one additional O, N, or S heteroatom;

R^{8b} and R^{9b} are each, independently, H or alkyl, or R^{8b} and R^{9b} taken together with the nitrogen atom to which they are attached form a 4- to 8-membered heterocycloalkyl ring wherein the heterocycloalkyl ring is optionally interrupted with one additional O, N, or S heteroatom;

R^{8c} and R^{9c} are each, independently, H or alkyl, or R^{8c} and R^{9c} taken together with the nitrogen and carbon atoms through which they are connected form a 4- to 8-membered heterocycloalkyl ring, wherein the heterocycloalkyl ring is optionally interrupted with one additional O, N, or S heteroatom;

R^{10} is $-(C(R^{14})(R^{15}))_q\text{-}R^{16}$;

R^{11} and R^{12} are each, independently, H or $-C(R^{14})(R^{15})R^{10}$;

R^{13} is $-OR^{14}$ or $-NR^{14}R^{15}$;

R^{14} and R^{15} are each, independently, H or alkyl;

R^{16} is H, alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, $-CR^{14}R^{15}OH$, $-CR^{14}R^{15}S(O)_rR^9$, $-CR^{14}R^{15}COOR^4$, $-CR^{14}R^{15}CONHR^4$, $-CR^{14}R^{15}NHR^4$, or $-CR^{14}R^{15}NH(C=NH)NH_2$;

Y is heteroaryl;

Z is H or $-OR^8$;

m is the integer 0 or 1;

n is an integer from 1 to 4;

o is an integer from 0 to 16;

p is an integer from 0 to 3;

q is an integer from 0 to 6; and

r is the integer 0, 1 or 2.

2. A compound according to claim 1,

wherein R^1 and R^2 are each, independently, H or alkyl.

3. A compound according to claim 2,

wherein R^1 and R^2 are each H.

4. A compound according to claim 1,

wherein each J is, independently, the amino acid glycine, phenylalanine, leucine, alanine, arginine, lysine, isoleucine, proline, tryptophan, serine, methionine, threonine, tyrosine, histidine, aspartic acid, cysteine, or (N-methyl)phenylalanine.

5. A compound according to claim 4,

wherein each J is, independently, the amino acid phenylalanine, arginine, lysine, proline, or tryptophan.

6. A compound according to claim 4,

wherein each J is, independently, the amino acid glycine, phenylalanine, leucine, or alanine.

7. A compound according to claim 4,

wherein each J is, independently, the amino acid serine, glycine, phenylalanine, leucine, or threonine.

8. A compound according to claim 4,

wherein R^3 is –[arg-Phe-Lys]-X,

–[Pro-Trp-Phe]-X,

–[Gly-Gly-Phe-Leu]-X,

–[ala-Gly-Phe-Leu]-X,

–[ala-Gly-N(CH_3)Phe]-X,

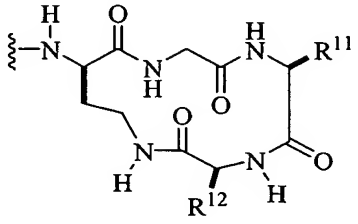
–[ser-Gly-Phe-Leu-Thr]-X,

–[ala-Phe-Gly-Tyr-Pro-Ser]-X, or

–[Gly-Gly-Phe-Leu-Arg-Arg-Ile-Arg-Pro-Lys]-X.

9. A compound according to claim 1,

wherein R^3 is: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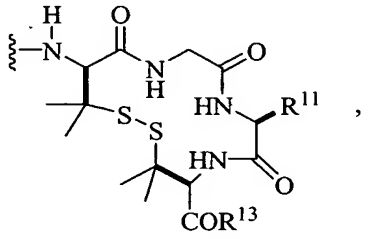
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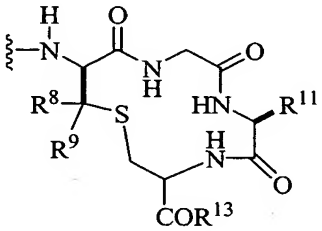
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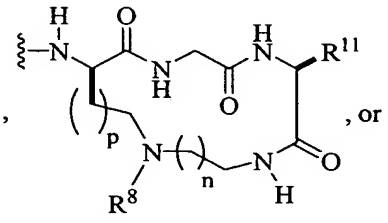
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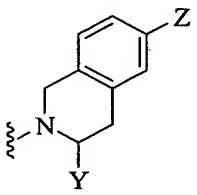
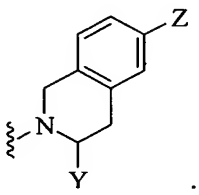


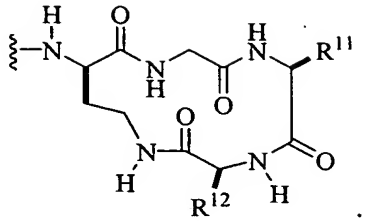
10. A compound according to claim 9,

wherein R^3 is:



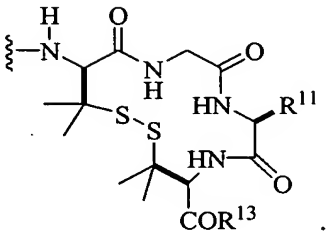
11. A compound according to claim 9,

wherein R^3 is:



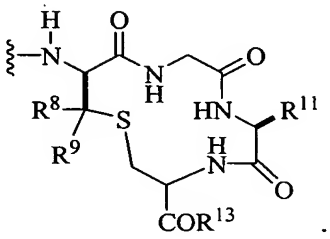
12. A compound according to claim 9,

wherein R^3 is:



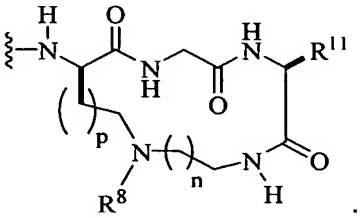
13. A compound according to claim 9,

wherein R^3 is:



14. A compound according to claim 9,

wherein R^3 is:



15. A compound according to claim 1,

wherein X is –OH, $-NH_2$, or $-NHCH_2CH_2OH$.

16. A compound according to claim 15,
wherein X is –OH or $-NH_2$.

17. A compound according to claim 16,
wherein X is $-NH_2$.

18. A compound according to claim 1,
wherein at least one of R^4 and R^5 is H.

19. A compound according to claim 1,
wherein R^6 and R^7 are each, independently, H or alkyl.

20. A compound according to claim 9,
wherein R^6 and R^7 are each H.

21. A compound according to claim 1,
wherein R^1, R^2, R^4, R^5, R^6, and R^7 are each H.

22. A compound according to claim 1,
wherein R^8 and R^9 are each, independently, H or alkyl.

23. A compound according to claim 22,
wherein R^8 and R^9 are each H.

24. A compound according to claim 22,
wherein R^8 and R^9 are each methyl.

25. A compound according to claim 1,
wherein R^{8a} and R^{9a} are each, independently, H or alkyl.

26. A compound according to claim 25,
wherein R^{8a} and R^{9a} are H.

27. A compound according to claim 1,

wherein R^{8a} and R^{9a} taken together with the nitrogen and carbon atoms through which they are connected form a 4- to 14-membered heterocycloalkyl ring wherein the heterocycloalkyl ring is optionally interrupted with one additional O, N, or S heteroatom, provided that the additional heteroatom is separated by at least two carbon atoms from the nitrogen atom to which R^{8a} is attached.

28. A compound according to claim 1,
wherein R^{8b} and R^{9b} are each, independently, H or alkyl.

29. A compound according to claim 1,
wherein R^{8c} and R^{9c} are each, independently, H or alkyl.

30. A compound according to claim 1,
wherein R^{10} is H.

31. A compound according to claim 1,
wherein R^{11} is aralkyl.

32. A compound according to claim 31,
wherein R^{11} is benzyl.

33. A compound according to claim 1,
wherein R^{12} is alkyl.

34. A compound according to claim 33,
wherein R^{12} is 2-methylprop-1-yl.

35. A compound according to claim 1,
wherein R^{13} is–OH or NH_2.

36. A compound according to claim 35,
wherein R^{13} is -OH.

37. A compound according to claim 1,

wherein Y is imidazol-2-yl or oxazol-2-yl.

38. A compound according to claim 1,
wherein Z is H or -OH.

39. A compound according to claim 1,
wherein m is 1.

40. A compound according to claim 1,
wherein n is 1.

41. A compound according to claim 1,
wherein o is 0 to 10.

42. A compound according to claim 41,
wherein o is 1 to 10.

43. A compound according to claim 42,
wherein o is 1 to 6.

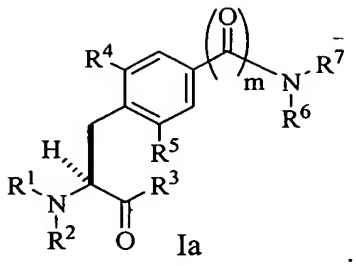
44. A compound according to claim 43,
wherein o is 1 to 4.

45. A compound according to claim 1,
wherein p is 1.

46. A compound according to claim 1,
wherein q is 0, 1 or 2.

47. A compound according to claim 1,
wherein r is 0.

48. A compound according to claim 1 of formula Ia:



Ia

49. A compound according to claim 1, wherein R^3 is:

$$[NR^{8d}(C(R^{9d})(R^{10}))_n\text{-}C(=O)]_s\text{-}J\text{-}[\ NR^{8e}(C(R^{9e})(R^{10}))_n\text{ -}C(=O)]_t\text{-}X;$$

wherein:

R^{8d} and R^{9d} are each, independently, H or alkyl, or R^{8d} taken together with the R^{9d} on the carbon atom *alpha* to the nitrogen bearing the R^{8d} and the nitrogen and carbon atoms through which they are connected form a 4- to 14-membered heterocycloalkyl ring wherein the heterocycloalkyl ring is optionally interrupted with one additional O, N, or S heteroatom;

R^{8e} and R^{9e} are each, independently, H or alkyl, or R^{8e} taken together with the R^{9e} on the carbon atom *alpha* to the nitrogen bearing the R^{8e} and the nitrogen and carbon atoms through which they are connected form a 4- to 8-membered heterocycloalkyl ring wherein the heterocycloalkyl ring is optionally interrupted with one additional O, N, or S heteroatom; and

the sum of s + t is an integer of 0 to 9.

50. A compound according to claim 49,

wherein the sum of s + t is 0 to 2.

51. A compound according to claim 50,

wherein the sum of s + t is 0 or 1.

52. A compound according to claim 51,

wherein s and t are 0.

53. A compound according to claim 49,

wherein J is $[NR^{8a}(CH(R^{9a})_n\text{-}C(=O)]$.

54. A compound according to claim 53,

wherein n is 1.

55. A compound according to claim 53,

wherein R^{8a} is H.

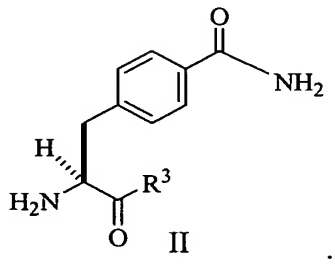
56. A compound according to claim 53,

wherein R^{9a} is H, benzyl, $-(CH_2)_4-NH_2$, CH_2-indol-3-yl, $-(CH_2)_3-NH-C(=NH)NH_2$, $-CH_2CH(CH_3)_2$, $-CH_3$, $-CH_2OH$, $-CH(OH)CH_3$, (*para*-hydroxyphenyl)methyl-, or $-CH(CH_3)CH_2CH_3$, or R^{8a} and R^{9a} taken together with the nitrogen and carbon atoms through which they are connected form a 4- to 14-membered heterocycloalkyl ring, wherein the heterocycloalkyl ring is optionally interrupted with one additional O, N, or S heteroatom.

57. A compound according to claim 56,

wherein R^{9a} is benzyl, $-(CH_2)_4-NH_2$, CH_2-indol-3-yl, or $-(CH_2)_3-NH-C(=NH)NH_2$,, or R^{8a} and R^{9a} taken together with the nitrogen and carbon atoms through which they are connected form a 4- to 8-membered heterocycloalkyl ring wherein the heterocycloalkyl ring is optionally interrupted with one additional O, N, or S heteroatom.

58. A compound according to claim 1 of formula II:



II

59. A compound according to claim 1, wherein said compound is:

H-(S)-2-Amino-3-(4-carboxamidophenyl)propionic acid-Gly-Gly-Phe-Leu-NH;

H-(S)-2-Amino-3-(4-carboxamidophenyl)propionic acid-Gly-Gly-Phe-Leu;

H-(S)-2-Amino-3-(4-carboxamidophenyl)propionic acid-ala-Gly-Phe-leu;

H-(S)-2-Amino-3-(4-carboxamidophenyl)propionic acid-ala-Gly-Phe-leu-NH_2;

H-(S)-2-Amino-3-(4-carboxamidophenyl)propionic acid-Gly-Gly-Phe-leu-NH_2;

H-(S)-2-Amino-3-(4-carboxamidophenyl)propionic acid-Arg-Phe-Lys-NH_2;

H-(S)-2-Amino-3-(4-carboxamidophenyl)propionic acid-arg-Phe-Lys-NH_2;

H-(S)-2-Amino-3-(4-carboxamidophenyl)propionic acid-Pro-Trp-Phe-NH_2;

H-(S)-2-Amino-3-(4-carboxamidophenyl)propionic acid-ala-Phe-Gly-Tyr-Pro-Ser;

H-(S)-2-Amino-3-(4-carboxamidophenyl)propionic acid-met-Phe-His-Leu-Met-Asp;

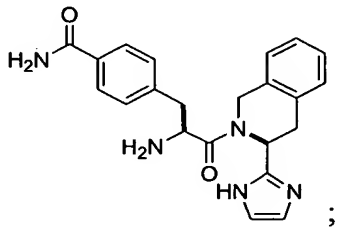
H-(S)-2-Amino-3-(4-carboxamidophenyl)propionic acid-ser-Gly-Phe-Leu-Thr;

H-(S)-2-Amino-3-(4-carboxamidophenyl)propionic acid-Gly-Gly-Phe-Leu-Arg-Arg-Ile-Arg-Pro-Lys;

H-(S)-2-Amino-3-(4-carboxamidophenyl)propionic acid-ala-Gly-N(Me)Phe-$NHCH_2CH_2OH$;

(S)-2-Amino-3-(4-carboxamidophenyl)propionic acid-c[D-A_2bu-Gly-Phe-Leu];

(S)-2-Amino-3-(4-carboxamidophenyl)propionic acid-c[D-Val_L-Gly-Phe-D-Ala_L]-OH;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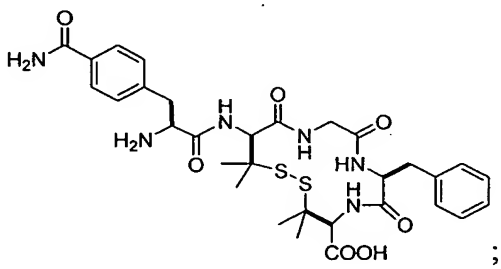
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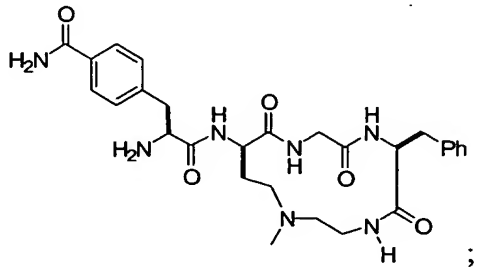
;

or a stereoisomer, prodrug, pharmaceutically acceptable salt, hydrate, solvate, acid salt hydrate, N-oxide or isomorphic crystalline form thereof.

60. A pharmaceutical composition, comprising:

a pharmaceutically acceptable carrier; and

an effective amount of a compound according to claim 1.

61. A pharmaceutical composition according to claim 60, further comprising:

an effective amount of at least one opioid.

62. A pharmaceutical composition according to claim 61,

wherein said opioid is selected from the group consisting of alfentanil, allylprodine, alphaprodine, anileridine, benzyl-morphine, bezitramide, buprenorphine, butorphanol, clonitazene, codeine, cyclazocine, desomorphine, dextromoramide, dezocine, diampromide, diamorphone, dihydrocodeine, dihydromorphine, dimenoxadol, dimepheptanol, dimethylthiambutene, dioaphetylbutyrate, dipipanone, eptazocine, ethoheptazine, ethylmethylthiambutene, ethylmorphine, etonitazene, fentanyl, heroin, hydrocodone, hydromorphone, hydroxypethidine, isomethadone, ketobemidone, levallorphan, levorphanol, levophenacylmorphan, lofentanil, meperidine, meptazinol, metazocine, methadone, metopon, morphine, myrophine, nalbuphine, narceine, nicomorphine, norlevorphanol, normethadone, nalorphine, normorphine, norpinanone, opium, oxycodone, oxymorphone, papaveretum, pentazocine, phenadoxone, phenomorphan, phanazocine, phenoperidine, piminodine, piritramide, propheptazine, promedol, properidine, propiram, propoxyphene, sulfentanil, tilidine, tramadol, diastereoisomers thereof, pharmaceutically acceptable salts thereof, complexes thereof and mixtures thereof.

63. A pharmaceutical composition according to claim 60, further comprising:

an effective amount of at least one compound selected from the group consisting of:

antibiotics, antivirals, antifungals, anti-inflammatories, anesthetics and mixtures thereof.

64. A method of binding opioid receptors in a patient in need thereof, comprising the step of:

administering to said patient an effective amount of a compound according to claim 1.

65. A method according to claim 64,

wherein said compound binds δ opioid receptors.

66. A method according to claim 65,

wherein said δ opioid receptors are located in the central nervous system.

67. A method according to claim 65,

wherein said δ opioid receptors are located peripherally to the central nervous system.

68. A method according to claim 64,

wherein said binding modulates the activity of said opioid receptors.

69. A method according to claim 68,

wherein said binding agonizes the activity of said opioid receptors.

70. A method according to claim 64,

wherein said compound does not substantially cross the blood-brain barrier.

71. A method according to claim 64,

wherein said patient is in need of prevention or treatment of a condition or disease caused by an opioid.

72. A method according to claim 71,

wherein said opioid is endogenous.

73. A method according to claim 71,

wherein said opioid is exogenous.

74. A method of preventing or treating pain, comprising the step of:

administering to a patient in need thereof an effective amount of a compound according to claim 1.

75. A method according to claim 74, further comprising the step of:

administering to said patient an effective amount of an opioid.

76. A method according to claim 75,

wherein said opioid is selected from the group consisting of alfentanil, allylprodine, alphaprodine, anileridine, benzyl-morphine, bezitramide, buprenorphine, butorphanol, clonitazene, codeine, cyclazocine, desomorphine, dextromoramide, dezocine, diampromide, diamorphone, dihydrocodeine, dihydromorphine, dimenoxadol, dimepheptanol, dimethylthiambutene, dioaphetylbutyrate, dipipanone, eptazocine, ethoheptazine, ethylmethylthiambutene, ethylmorphine, etonitazene, fentanyl, heroin, hydrocodone, hydromorphone, hydroxypethidine, isomethadone, ketobemidone, levallorphan, levorphanol, levophenacylmorphan, lofentanil, meperidine, meptazinol, metazocine, methadone, metopon, morphine, myrophine, nalbuphine, narceine, nicomorphine, norlevorphanol, normethadone, nalorphine, normorphine, norpinanone, opium, oxycodone, oxymorphone, papaveretum, pentazocine, phenadoxone, phenomorphan, phanazocine, phenoperidine, piminodine, piritramide, propheptazine, promedol, properidine, propiram, propoxyphene, sulfentanil, tilidine, tramadol, diastereoisomers thereof, pharmaceutically acceptable salts thereof, complexes thereof and mixtures thereof.

77. A method for preventing or treating gastrointestinal dysfunction, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

78. A method for preventing or treating ileus, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

79. A method for preventing or treating a urogenital tract disorder, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

80. A method according to claim 79,

wherein said urogenital tract disorder is incontinence.

81. A method of preventing or treating an immunomodulatory disorder, comprising the step of:

administering to a patient in need thereof an effective amount of a compound according to claim 1.

82. A method according to claim 81,

wherein said immunomodulatory disorder is selected from the group consisting of:

an autoimmune disease, a collagen disease, an allergy, a side effect associated with the administration of an anti-tumor agent, and a side effect associated with the administration of an antiviral agent.

83. A method according to claim 82,

wherein said autoimmune disease is selected from the group consisting of:

arthritis, an autoimmune disorder associated with a skin graft, an autoimmune disorder associated with organ transplant, and an autoimmune disorder associated with surgery.

84. A method for preventing or treating an inflammatory disorder, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

85. A method according to claim 84,

wherein said inflammatory disorder is arthritis, psoriasis, asthma, or inflammatory bowel disease.

86. A method for preventing or treating a respiratory function disorder, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

87. A method according to claim 86,

wherein said respiratory function disorder is asthma or lung edema.

88. A method for preventing or treating anxiety, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

89. A method for preventing or treating a mood disorder, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

90. A method according to claim 89, wherein said mood disorder is depression, bipolar manic-depression, or seasonal affective disorder.

91. A method for preventing or treating a stress-related disorder, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

92. A method according to claim 91,

wherein said stress-related disorder is post-traumatic stress disorder, panic disorder, generalized anxiety disorder, social phobia, or obsessive compulsive disorder.

93. A method for preventing or treating attention deficit hyperactivity disorder, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

94. A method for preventing or treating sympathetic nervous system disorder, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

95. A method according to claim 94,

wherein said sympathetic nervous system disorder is hypertension.

96. A method for preventing or treating tussis, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

97. A method for preventing or treating a motor disorder, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

98. A method according to claim 97,

wherein said motor disorder is tremors, Parkinson's disease, or Tourette syndrome.

99. A method for treating a traumatic injury to the central nervous system, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

100. A method according to claim 99,

wherein said traumatic injury is traumatic injury to the spinal cord or brain.

101. A method for preventing or treating stroke, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

102. A method for preventing or treating cardiac arrhythmia, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

103. A method for preventing or treating glaucoma, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

104. A method for preventing or treating sexual dysfunction, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

105. A method according to claim 104,

wherein said sexual dysfunction is premature ejaculation.

106. A method for treating a condition selected from the group consisting of shock, brain edema, cerebral ischemia, cerebral deficits subsequent to cardiac bypass surgery and grafting, systemic lupus erythematosus, Hodgkin's disease, Sjogren's disease, epilepsy, and rejection in organ transplants and skin grafts, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

107. A method for treating substance addiction, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

108. A method according to claim 107,

wherein said substance addiction is alcohol addiction, nicotine addiction or drug addiction.

109. A method according to claim 108,

wherein said drug addiction is addiction to opioids.

110. A method for improving organ and cell survival, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

111. A method for providing cardioprotection following myocardial infarction, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

112. A method for reducing the need for anesthesia, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

112. A method of producing or maintaining an anesthetic state, comprising the step of:

administering to a patient in need of such treatment an effective amount of a compound according to claim 1.

114. A method according to claim 113, further comprising the step of:

administering to said patient an anesthetic agent selected from the group consisting of an inhaled anesthetic, a hypnotic, an anxiolytic, a neuromuscular blocker and an opioid.

115. A method according to claim 114,

wherein said compound and said anesthetic agent are co-administered.

116. A compound according to claim 1 which is radio-labeled.

117. A compound according to claim 1 which is isotopically-labeled.